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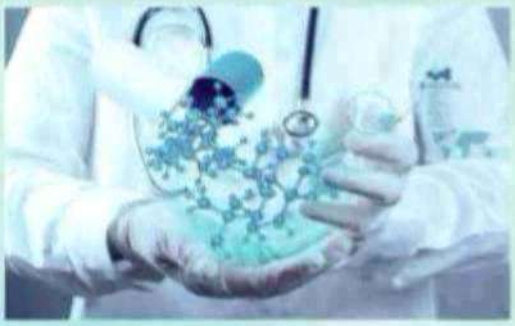

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OPIOID-SPARING ANALGESIA AND DEXMEDETOMIDINE SEDATION DURING CESAREAN SECTION UNDER SPINAL ANESTHESIA

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✓ ***Resume***

The aim of this study was to optimize the efficacy of dexmedetomidine (DEX)-based medication sedation on the background of spinal anesthesia (SA) in pregnant women undergoing cesarean section (CS) and to evaluate its impact on postoperative cognitive dysfunction (POCD). The study included 200 women at risk of POCD who underwent elective CS between 2021 and 2024. Patients were divided into a main group (n=100, DEX sedation without opioids) and a control group (n=100, sedation with ketamine, propofol, diazepam, or sodium oxybutyrate). Hemodynamics, respiration, psychoemotional status (RASS, BIS, MMSE, MoCA-test), and neonatal condition (Apgar, NACS) were assessed. DEX provided light-to-moderate sedation in 95% of cases without POCD development in 98%, reduced maternal and fetal complications, and minimized impact on neonatal vital systems (86% without depression). DEX demonstrated a pronounced opioid-sparing effect. An optimal regimen was developed: bolus 1 μg/kg followed by infusion 0.5–1 μg/kg/h. DEX is a safe and effective agent for opioid-sparing analgesia and sedation in CS, preventing POCD and improving perinatal outcomes.

Keywords: Dexmedetomidine, spinal anesthesia, cesarean section, sedation, opioid-sparing analgesia, postoperative cognitive dysfunction.

SPINAL ANESTEZIYA PAYTIDA KESARCHA KESISHDA OPIOID TEJOVCHI ANALGEZIYA VA DEKSMEDETOMIDIN SEDATSIYASI

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✓ ***Rezyume***

Ushbu tadqiqotning maqsadi — homilador ayollarda spinal anesteziya (SA) fonida deksmedetomidin (DEX) asosidagi se dat siyani samaradorligini optimallashtirish va uning operatsiyadan keyingi kognitiv disfunktsiyaga (OKD) ta’sirini baholash edi. Tadqiqotga 2021–2024 yillarda rejalashtirilgan kesarcha kesish (KK) o‘tkazilgan, OKD rivojlanish xavfi yuqori bo‘lgan 200 nafar ayol kiritildi. Bemorlar asosiy guruhga (n=100, opioid siz DEX sedatsiyasi) va nazorat guruhiga (n=100, ketamin, propofol, diazepam yoki natriy oksibutirat bilan sedatsiya) bo‘lingan. Gemodinamika, nafas olish, psixoemotsional holat (RASS, BIS, MMSE, MoCA testi), shuningdek, yangi tug‘ilgan chaqaloqlar holati (Apgar, NACS) baholandi. DEX 95% hollarda yengil–o‘rtacha sedatsiyani ta’minladi, 98% hollarda OKD rivojlanmadi, ona va homila asoratlarini kamaytirdi, yangi tug‘ilganlarning hayotiy tizimlariga ta’sirini minimallashtirdi (86% depressiyasiz). Deksmedetomidin aniq opioid tejovchi ta’sir ko‘rsatdi. Optimal rejim ishlab chiqildi: bolus 1 mkg/kg, keyin infuziya 0,5–1 mkg/kg/soat. Deksmedetomidin kesarcha kesishda opioid tejovchi analgeziya va sedatsiya uchun xavfsiz va samarali vosita bo‘lib, OKD ning oldini oladi va perinatal natijalarni yaxshilaydi.

Kalit so‘zlar: Deksmedetomidin, spinal anesteziya, kesarcha kesish, sedatsiya, opioid tejovchi analgeziya, operatsiyadan keyingi kognitiv disfunktsiya.

БЕЗОПИОИДНАЯ АНАЛЬГЕЗИЯ С ПРИМЕНЕНИЕМ ДЕКСМЕДЕТОМИДИНА ДЛЯ СЕДАЦИИ ПРИ КЕСАРЕВОМ СЕЧЕНИИ В УСЛОВИЯХ СПИНАЛЬНОЙ АНЕСТЕЗИИ

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✓ ***Резюме***

Цель исследования — оптимизировать эффективность седации на основе дексмедетомидина (DEX) на фоне спинальной анестезии (СА) у беременных женщин, подвергающихся кесареву сечению (КС), и оценить её влияние на послеоперационную когнитивную дисфункцию (ПОКД). В исследование включены 200 женщин с риском развития ПОКД, перенесших плановое КС в период 2021–2024 гг. Пациентки были разделены на основную группу (n=100, седация DEX без опиоидов) и контрольную группу (n=100, седация кетамином, пропофолом, диазепамом или натрия оксибутиратом). Оценивались гемодинамика, дыхание, психоэмоциональное состояние (RASS, BIS, MMSE, тест MoCA), а также состояние новорождённых (Apgar, NACS). DEX обеспечивал лёгкую–умеренную седацию в 95% случаев без развития ПОКД в 98%, снижал материнские и фетальные осложнения, минимизировал влияние на жизненно важные системы новорождённых (86% без депрессии). Дексмедетомидин продемонстрировал выраженный опиоид-сберегающий эффект. Разработан оптимальный режим: болюс 1 мкг/кг с последующей инфузией 0,5–1 мкг/кг/ч. Дексмедетомидин является безопасным и эффективным средством для опиоид-сберегающей анальгезии и седации при КС, предотвращает ПОКД и улучшает перинатальные исходы.

Ключевые слова: Дексмедетомидин, спинальная анестезия, кесарево сечение, седация, безопиоидная анальгезия, послеоперационная когнитивная дисфункция.

Relevance

Cesarean section (CS) remains one of the most frequently performed surgical procedures in obstetrics, with rates ranging from 15–25% in specialized centers to over 50% in high-risk perinatal facilities [1]. The increasing frequency of CS is associated with elevated maternal morbidity and mortality, where anesthesia-related complications, massive hemorrhage, and infections are leading causes of fatal outcomes [2]. In contemporary practice, the choice of anesthetic technique for CS must ensure reliable protection of the parturient from surgical stress while promoting optimal fetal adaptation in the peri- and neonatal periods.

Spinal anesthesia (SA) is recognized as the gold standard for elective CS, providing rapid and reliable sensory and motor blockade, minimal impact on maternal physiological functions, preservation of consciousness, and a substantially reduced risk of aspiration and fetal depression compared to general anesthesia [3]. Despite these advantages, the majority of parturients experience significant anxiety, fear, and discomfort during the procedure, necessitating adequate pharmacological sedation [4].

Traditional sedative agents (midazolam, propofol, ketamine, sodium oxybutyrate) and opioid adjuvants (morphine, fentanyl) carry substantial drawbacks, including respiratory depression, hemodynamic instability, fetal effects, postoperative nausea/vomiting, and risk of post-traumatic stress disorder [5]. Furthermore, postoperative cognitive dysfunction (POCD) — characterized by impairment in memory, attention, executive function, and orientation — remains an underappreciated issue, particularly in parturients with repeated CS, uterine scar, and high psychoemotional stress [6].

POCD after CS is particularly relevant: early cognitive impairment occurs more frequently after general anesthesia, yet even with regional techniques, incidence may reach 10–20% in the first days to week postoperatively, especially in patients with reduced cognitive reserve [7]. Recent meta-analyses confirm that perioperative dexmedetomidine significantly reduces POCD incidence (OR 0.47–0.59),

lowers inflammatory markers, and improves MMSE/MoCA scores in the early postoperative period [8].

Dexmedetomidine, a highly selective α_2-adrenoceptor agonist, provides sedative, anxiolytic, analgesic, and sympatholytic effects without significant respiratory depression, inducing a state resembling natural sleep. In obstetric practice, DEX is increasingly used as an adjuvant to SA: intravenous administration prolongs sensory and motor blockade, reduces opioid requirements, and ensures hemodynamic stability. Its lack of depressive effects on the fetus, opioid-sparing properties, and potential neuroprotective action make DEX particularly attractive for parturients at risk of POCD [9].

In the Republic of Uzbekistan, the expansion of maternal and child healthcare and the national priorities for maternal and child protection underscore the need for safe, opioid-sparing sedation and analgesia methods in CS. Despite growing evidence of DEX's neuroprotective properties, questions regarding optimal dosing, effects on cognitive function, and perinatal outcomes in parturients at risk of POCD under regional anesthesia remain insufficiently addressed in regional settings [10].

The aim of the study was to evaluate the efficacy and safety of opioid-sparing analgesia and dexmedetomidine sedation on the background of spinal anesthesia during cesarean section in pregnant women at risk of postoperative cognitive dysfunction, and to develop an optimal drug administration regimen.

Materials and methods

The study was conducted in the obstetrics department of the multidisciplinary clinic of Samarkand State Medical University and the branch of the Republican Specialized Scientific-Practical Medical Center for Maternal and Child Health in Samarkand region between 2021 and 2024. The study population comprised 200 pregnant women at risk of postoperative cognitive dysfunction (POCD) (age 18–40 years, gestational age 37–40 weeks) undergoing elective cesarean section (CS). Inclusion criteria: ASA physical status I–II, no contraindications to spinal anesthesia (SA), POCD risk confirmed by preoperative MMSE score <27 and/or MoCA-test score <26. Exclusion criteria: emergency CS, severe somatic comorbidities, known allergy to study medications.

Patients were randomized into two groups:

Main group (n = 100) — sedation with dexmedetomidine (DEX) without opioids;

Control group (n = 100) — sedation with one of four alternative agents, further divided into four equal subgroups (n = 25 in each):

Subgroup K — ketamine (bolus 0.5 mg/kg, followed by infusion if needed);

Subgroup P — propofol (target-controlled infusion or 1–2 mg/kg/h);

Subgroup D — diazepam (0.1–0.2 mg/kg bolus, repeated as required);

Subgroup O — sodium oxybutyrate (20–40 mg/kg bolus).

All patients received standard premedication with atropine 0.01 mg/kg i.v. Spinal anesthesia was performed with hyperbaric bupivacaine 10–12 mg intrathecally at the L3–4 or L2–3 interspace. In the main group, after confirming adequate block level, DEX was administered as an initial bolus of 1 μg/kg over 10 minutes, followed by continuous infusion of 0.5–1.0 μg/kg/h until the end of surgery. No opioids were used intraoperatively or in the early postoperative period in this group. In the control subgroups, the respective sedative was started after SA and titrated to achieve a Richmond Agitation-Sedation Scale (RASS) score of –2 to –3.

Assessment methods included:

Hemodynamic monitoring (non-invasive BP, HR, SpO_2, RR);

Depth of sedation — Richmond Agitation-Sedation Scale (RASS) and Bispectral Index (BIS);

Cognitive function — Mini-Mental State Examination (MMSE) and Montreal Cognitive Assessment (MoCA) performed 1 day before surgery and on postoperative days 1 and 3;

Neonatal condition — Apgar score at 1 and 5 minutes, Neurologic and Adaptive Capacity Score (NACS) at 2 hours of life;

Biochemical markers of stress — plasma cortisol and norepinephrine (selected time points).

Statistical analysis was performed using SPSS 26.0. Normality tested by Shapiro-Wilk. Comparisons: Student's t-test for parametric data, Mann-Whitney U-test for nonparametric.

Categorical variables were compared using χ^2 test or Fisher's exact test. Differences were considered statistically significant at $p < 0.05$. Data are presented as mean ± standard deviation (M ± SD) unless otherwise specified.

The study protocol was approved by the Ethics Committee of Samarkand State Medical University (No. 012000261 dated March 12, 2024). Written informed consent was obtained from all participants.

Results and discussion

In the main (DEX) group, hemodynamics remained remarkably stable throughout the procedure: mean systolic blood pressure decreased by 10–15% from baseline without clinically significant hypotension, heart rate ranged 70–80 bpm. Respiratory parameters were preserved ($SpO_2 \geq 98\%$, respiratory rate 16–18/min) with no episodes of desaturation or hypoventilation.

In the control group, hemodynamic instability was more pronounced (Table 1), particularly in the ketamine (K) and propofol (P) subgroups:

Hypotension (systolic BP <90 mmHg) occurred in 28% of propofol cases, 20% of ketamine cases, 12% of diazepam cases, and 8% of sodium oxybutyrate cases ($p < 0.05$ vs. DEX for P and K subgroups);

Tachycardia (>100 bpm) was most frequent in the ketamine subgroup (36%) compared to 4% in the DEX group ($p < 0.001$).

Overall, dexmedetomidine provided clearly better preservation of hemodynamic and respiratory stability than all four alternative sedatives, with the most pronounced differences observed against propofol and ketamine.

Table 1.

Intraoperative hemodynamic parameters (M ± SD)

Parameter	DEX (n=100)	Ketamine (n=25)	Propofol (n=25)	Diazepam (n=25)	Oxybutyrate (n=25)	p (DEX vs. all controls)
Systolic BP (mmHg)	110 ± 10	102 ± 14	98 ± 13	108 ± 11	112 ± 9	<0.05 (vs. K, P)
Heart rate (bpm)	75 ± 8	92 ± 12	84 ± 10	78 ± 9	76 ± 8	<0.001 (vs. K)
SpO_2 (%)	99 ± 1	97 ± 2	96 ± 3	98 ± 1	98 ± 2	<0.05 (vs. P)

Sedation quality (RASS –2 to –3) was achieved and maintained in 95% of DEX patients versus 78–84% across control subgroups ($p < 0.01$). BIS values remained in the target range (60–80) more consistently in the DEX group. Oversedation (RASS ≤ –4) was recorded in 20% of propofol patients and 16% of diazepam patients (Table 2). Dexmedetomidine provides markedly superior, more predictable, and tightly controllable sedation compared to conventional agents (ketamine, propofol, diazepam, sodium oxybutyrate). This advantage stems from DEX's unique ability to produce a physiologic, "natural sleep-like" state that preserves protective airway reflexes and spontaneous breathing — in clear contrast to other sedatives, which frequently result in greater variability in sedation depth and clinically significant oversedation (propofol 20%, diazepam 16%). These properties position dexmedetomidine as the preferred sedative agent in obstetric regional anesthesia, particularly for patients at risk of postoperative cognitive dysfunction.

Table 2.

Sedation depth parameters (intraoperative mean values, M ± SD)

Parameter	DEX (n=100)	Ketamine (n=25)	Propofol (n=25)	Diazepam (n=25)	Oxybutyrate (n=25)	p (DEX vs. all controls)
RASS score (main phase)	–2.4 ± 0.5	–2.1 ± 0.8	–2.6 ± 0.7	–2.0 ± 0.6	–2.2 ± 0.5	<0.05 (vs. P)
Patients with RASS –2 to –3 (%)	95%	80%	76%	84%	88%	<0.01
BIS value (mean)	72 ± 6	78 ± 8	65 ± 9	74 ± 7	76 ± 6	<0.05 (vs. P, K)
Oversedation (RASS ≤ –4) (%)	3%	8%	20%	16%	4%	<0.01 (vs. P, D)

Postoperative cognitive function showed the most favorable dynamics in the DEX group: MMSE increased from 25.6 ± 1.2 to 27.8 ± 0.9 and MoCA from 24.8 ± 1.1 to 26.5 ± 0.8 on day 1 ($p < 0.001$ vs. all control subgroups). POCD (≥2-point decline sustained to day 3) was diagnosed in only 2% of DEX patients compared to 16–28% across control subgroups (highest in propofol and ketamine subgroups, $p < 0.001$) (Table 3). This neuroprotective effect is likely multifactorial — reduced sympathetic hyperactivity, attenuated inflammatory response, and possible BDNF pathway modulation.

Table 3.

Postoperative cognitive scores on day 1 (M ± SD)

Scale	DEX (n=100)	Ketamine (n=25)	Propofol (n=25)	Diazepam (n=25)	Oxybutyrate (n=25)	p (DEX vs. all)
MMSE	27.8 ± 0.9	24.1 ± 1.4	23.8 ± 1.5	25.2 ± 1.2	25.6 ± 1.1	<0.001
MoCA	26.5 ± 0.8	23.0 ± 1.6	22.7 ± 1.7	24.1 ± 1.3	24.4 ± 1.2	<0.001
POCD (%)	2%	24%	28%	16%	12%	<0.001

Moreover, neonatal outcomes were significantly better in the DEX group: Apgar score at 1 min 8.2 ± 0.5 vs. 7.3–7.7 in control subgroups ($p < 0.01$); at 5 min 9.1 ± 0.3 vs. 8.4–8.8 ($p < 0.05$). NACS >35 points (excellent adaptation) was observed in 86% of DEX neonates versus 52–68% in control subgroups ($p < 0.01$) (Table 4). Thus, DEX showed no clinically significant depressive effect on the neonate, which aligns well with existing pharmacokinetic and clinical evidence demonstrating minimal placental transfer and preservation of normal fetal/neonatal physiology when dexmedetomidine is used intravenously during cesarean section under spinal anesthesia.

Table 4.

Neonatal outcomes (M ± SD)

Parameter	DEX (n=100)	Ketamine (n=25)	Propofol (n=25)	Diazepam (n=25)	Oxybutyrate (n=25)	p (DEX vs. all)
Apgar 1 min	8.2 ± 0.5	7.4 ± 0.7	7.3 ± 0.8	7.6 ± 0.6	7.7 ± 0.6	<0.01
Apgar 5 min	9.1 ± 0.3	8.5 ± 0.5	8.4 ± 0.6	8.7 ± 0.4	8.8 ± 0.4	<0.05
NACS (points)	37 ± 2	33 ± 4	32 ± 4	35 ± 3	35 ± 3	<0.01
NACS >35 (%)	86%	56%	52%	68%	64%	<0.01

The present study demonstrates clear advantages of dexmedetomidine (DEX) over conventional sedative agents (ketamine, propofol, diazepam, and sodium oxybutyrate) when used as an adjuvant to spinal anesthesia for elective cesarean section in parturients at risk of postoperative cognitive dysfunction (POCD).

Conclusions

Dexmedetomidine-based opioid-sparing sedation under spinal anesthesia during cesarean section provides superior hemodynamic stability, more consistent and predictable sedation depth, significantly lower incidence of postoperative cognitive dysfunction (only 2% vs. 12–28% in control subgroups), and better neonatal adaptation compared with ketamine, propofol, diazepam, or sodium oxybutyrate. Among the control agents, diazepam and sodium oxybutyrate demonstrated relatively better profiles than ketamine and propofol regarding hemodynamics and neonatal outcomes, but still inferior to dexmedetomidine in all measured domains. The recommended dexmedetomidine regimen (1 μg/kg bolus over 10 min followed by 0.5–1.0 μg/kg/h infusion) can be considered the optimal approach for parturients at risk of POCD undergoing elective cesarean section under spinal anesthesia.

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